**University of Leicester**

**BBSRC MIBTP Studentship Project 2024-5 entry.**

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| **Project Reference** |  |

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| **Additional Supervisor** |  |

**Section 2 – *Project Information***

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| **Project Title** | **Development of meal insects for the production of high value biologicals.** |
| **Project Summary** | |
| There is growing demand for biologically active compounds, especially proteins.  These can be used as valuable enzymes in production processes, may take the form of antibodies for the diagnosis and treatment of diseases, may function as antigens to elicit immune responses following vaccination, and may be engineered fibres with custom-build structural properties. In addition, production of mammalian food proteins (like those of milk) in non-mammalian edible systems (like insects) is seen by some as an ethically preferable food alternative, both in terms of animal welfare and of environmental costs.  This project is about developing insects as an efficient system for the production of valuable proteins. Long term, we aim to employ two species *Hermetia illucens* (a fly) and *Tenebrio molitor* (a beetle).  We choose these species because they are cheap and safe to grow, have a low carbon footprint and are equally easy to farm in developed and less developed countries. Both *Hermetia* (black soldier fly) and *Tenebrio* (mealworm) include in their development voracious larval stages that feed on a variety of organic materials, including waste (domestic, farm, and industrial). Both species are used for the production of larvae as animal feed and pet food. Additionally, mealworms are considered safe for human consumption (European Food Safety Authority). By using these species there is scope for converting organic waste into high value biologicals. Moreover, there is the potential of generating food containing antibodies or other protein therapeutics for the treatment of animal or even human disease by oral delivery.  To establish these species as a biomanufacturing platform we need:  (1) To build robust but flexible genetic tools  (a) to engineer transgenic strains  (b) to promote gene editing.  (2) To design protocols that optimise the production of the desired proteins (which may require post-translational modifications) while minimizing the metabolic and developmental toll on the host.  (a) finding the right tissue for expression  (b) finding the right timing for expression  (c) exploring strategies such as production of monomeric or multimeric variants, fusions with solubilisation partners, capping with signal peptides  (c) exploring strategies such as co-expression of chaperones, inhibitors, modifying enzymes, etc.  Clearly, the whole process (1+2) requires much more time than that available for a PhD.  We suggest (but we are open to discussion) to begin with (2). In fact, we can use a common model system, the fruit fly *Drosophila melanogaster*, to initiate the optimisation process. Using *Drosophila*, we have access to a formidable genetic toolkit that then we can adapt to the two other species once we have identified the best conditions for expression. As a starting point, we propose to use a battery of available nanobodies (antibodies that are 10 times smaller than conventional ones) and optimize their expression and purification strategies in comparison to the standard prokaryotic expression system, *E. coli*. Establishing *Drosophila* as a viable expression system for the productions of nanobodies will be a dramatic achievement *per se*, with possible translational implications. Further, it will constitute a fundamental stepping stone for establishing meal insects as a biomanufacturing platform.  Techniques that will be undertaken during the project  Molecular biology, cloning, PCR, gene expression, protein expression and purification, elisa, bioinformatics, databases, genetics, confocal microscopy. | |
| **References** | |
| Mealworm (Tenebrio molitor Larvae) as an Alternative Protein Source for Monogastric Animal: A Review. DOI: 10.3390/ani10112068.  Review of Black Soldier Fly (Hermetia illucens) as Animal Feed and Human Food. DOI: 10.3390/foods6100091.  Nanobodies: A Review of Generation, Diagnostics and Therapeutics. DOI: 10.3390/ijms24065994 | |

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